

Support for the new claims can be found throughout the instant case including the Drawings and claims as filed originally. No new matter has been added.

Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Attached to this submission is a marked-up version of the changes made to the specification and claims. The attached page is captioned "version with markings to show changes made".

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1, 1A, 2, 3, 5-15, 17-30, and 48 have been canceled.

The following new claims 49- 78 have been added.

49. (New) A method for inducing formation of new blood vessels in a mammal having chronic or acute ischemia, wherein the method comprises administering to the mammal an effective amount of a vascularization modulating agent sufficient to form the new blood vessels in the mammal, and increasing endothelial progenitor cell (EPC) frequency by at least about 20% as determined by a standard EPC isolation assay.

50. (New) The method of claim 49, wherein the vascularization modulating agent is GM-CSF, M-CSF, b-FGF, SCF, SDF-1, G-CSF, HGF, Angiopoietin1, Angiopoietin-2, FLT-3 ligand, or an effective fragment thereof.

51. (New) The method of claim 49, wherein the vascularization modulating agent is GM-CSF, and amount of the GM-CSF administered to the mammal is sufficient to increase frequency of endothelial progenitor cells (EPC) in the mammal.

52. (New) The method of claim 51, wherein the increase in frequency of the EPC is at least about 20% as determined by a standard EPC isolation assay.

53. (New) The method of claim 49, wherein the increase in EPC differentiation is at least about 20% as determined by a standard EPC culture 2 5 assay.

54. (New) The method of claim 49, wherein the amount of vascularization modulating agent administered to the mammal is sufficient to increase blood vessel length in the mammal.

55. (New) The method of claim 54, wherein the increase in blood vessel length is at least about 5% as determined by a standard blood vessel length assay.

56. (New) The method of claim 54, wherein the amount of vascularization modulating agent administered to the mammal is further sufficient to increase blood vessel diameter in the mammal.

57. (New) The method of claim 56, wherein the increase in blood vessel diameter is at least about 5% as determined by a standard blood vessel diameter assay.

58. (New) The method of claim 49, wherein the amount of vascularization modulating agent administered to the mammal is sufficient to increase EPC differentiation following tissue ischemia.

59. (New) The method of claim 58, wherein the increase in EPC differentiation is at least about 20% as determined by a standard hindlimb ischemia assay.

60. (New) The method of claim 49, wherein the amount of administered vascularization modulating agent is sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.

61. (New) The method of claim 49, wherein the amount of administered vascularization modulating agent is sufficient to increase EPC incorporation into foci.

62. (New) The method of claim 61, wherein the increase in EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.

63. (New) The method of claim 49, wherein the mammal has, is suspected of having, or will have ischemic tissue.

64. (New) The method of claim 63, wherein the ischemic tissue comprises tissue from a limb, graft, or organ.

65. (New) The method of claim 63, wherein the tissue is associated with the circulatory system or the central nervous system.

66. (New) The method of claim 63, wherein the tissue is heart or brain tissue.

67. (New) The method of claim 49, wherein the is co-administered with at least one angiogenic protein.

68. (New) The method of claim 49, wherein the agent is co-administered with at least one angiogenic protein.

69. (New) The method of claim 67, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TGF- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxide synthase (NOS); or a fragment thereof. -

70. (New) The method of claim 68, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TGF- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxide synthase (NOS); or a fragment thereof.

71. (New) A method for preventing or reducing the severity of blood vessel damage in a mammal having chronic or acute ischemia, wherein the method comprises administering to the mammal an effective amount of granulocyte macrophage-colony stimulating factor (GM-CSF); and exposing the mammal having the chronic or acute ischemia to conditions conducive to damaging the blood vessels, the amount of GM-CSF being sufficient to prevent or reduce the severity of the blood vessel damage in the mammal.

72. (New) The method of claim 71, wherein the conditions conducive to the blood vessel damage are an invasive manipulation or ischemia.

73. (New) The method of claim 72, wherein the invasive manipulation is surgery.

74. (New) The method of claim 72, wherein the ischemic is associated with at least one of infection, trauma, graft rejection, cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy, or myocardial ischemia.

75. (New) The method of claim 71, wherein the GM-CSF is administered to the mammal at least about 12 hours before exposing the mammal to the conditions conducive to damaging the blood vessels.

76. (New) The method of claim 75, wherein the GM-CSF is administered to the mammal between from about 1 to 10 days before exposing the mammal to the conditions conducive to damaging the blood vessels.

77. (New) The method of claim 75, wherein the method further comprises administering the GM-CSF to the mammal following the exposure to the conditions conducive to damaging the blood vessels.

78. (New) A method for enhancing endothelial progenitor cell (EPC) mobilization in a mammal having chronic or acute ischemia, wherein the method comprises administering an

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effective amount of at least one hematopoietic factor sufficient to enhance the EPC mobilization
in the mammal having the chronic or acute ischemia.

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